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[Classification of Gastrointestinal Disease of Infants and Children Due to Adverse Immunologic Reactions to Foods Proceedings of a Workshop]

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ABSTRACT

Food Protein-Induced Enterocolitis Syndrome (FPIES) is a symptom complex of severe vomiting and diarrhea caused by non-IgE-mediated allergy to cow's milk and/or soy in infants. Symptoms typically begin in the first month of life in association with failure to thrive and may progress to acidemia and methemoglobinemia. Symptoms resolve after the causal protein (usually sensitivity to both cow's milk and soy) is removed from the diet. Symptoms recur approximately 2 hours after reintroduction of the protein along with a coincident elevation of the peripheral blood polymorphonuclear leukocyte count. The sensitivity is usually outgrown by 3 years of age. The purpose of this review is to delineate the characteristic clinical features, diagnosis and management of FPIES. Furthermore, infantile FPIES will be discussed in relation to clinical syndromes that share features with it ("atypical FPIES") and other food-allergic disorders affecting the gastrointestinal tract.

Food allergy, an immune-mediated disorder, affects 6% to 8% of infants less than 2 years of age (1). The most common dietary proteins responsible for food-allergic reactions in these infants are cow's milk and soybean, with cow's milk allergy (CMA) accounting for approximately 2.5% of the allergic responses (1-4). The clinical manifestations of food allergy include acute reactions (e.g., hives, asthma, and anaphylaxis) and chronic, indolent disease (e.g., failure to thrive, diarrhea, and atopic dermatitis) (5). These disorders may be divided on an immunologic basis into those that are mediated by IgE antibody directed toward the specific causal protein and those that are not IgE mediated. In general, food-allergic disorders affecting only the gut are non-IgE mediated (with the exception of subsets of children with "gastrointestinal anaphylaxis," eosinophilic gastroenteritis, and malabsorption associated with atopic dermatitis [6]). Fortunately, 85% to 90% of infants with CMA show tolerance by 3 years of age (2,7,8).

Among the food-allergic disorders affecting the gastrointestinal tract, there are a myriad of clinical manifestations (vomiting, diarrhea, growth failure, abdominal pain) and a broad range of severity and chronicity. Clinical-histopathologic correlation includes a variety of findings with varying degrees and types of inflammation. Some food-allergic disorders affecting the gut have been well delineated (celiac disease [9]). However, many of these disorders (e.g., enteropathy syndrome, gastroesophageal reflux, eosinophilic gastroenteritis, and others) remain less well defined, may represent a spectrum of disorders, are often "lumped" together in clinical reviews, and probably represent a number of immunopathophysiologic causes. The primary feature common to the food-allergic disorders affecting the gut is that elimination of the offending food protein results in resolution of the clinical symptoms (and normalization of histologic abnormalities), reintroduction of the causal protein results in recurrence of these abnormalities, and no other cause (infection, intolerance) is identifiable (10).

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Food protein-induced enterocolitis syndrome (FPIES) describes a symptom complex of profuse vomiting and diarrhea diagnosed in infancy (11-13). Because both the small and large bowel are involved, the term enterocolitis is used. Although the clinical syndrome may represent a more severe form of food protein-induced enteropathy (abdominal symptoms, malabsorption with associated villous blunting (14)), there are particular features including signs of systemic reactivity and implications for long-term clinical management that warrant its discussion as a distinct clinical entity. The purpose of this review is to delineate the characteristic clinical features, diagnosis, and management of FPIES. Furthermore, infantile FPIES will be discussed in relation to other clinical syndromes that share features with it (atypical FPIES). Finally, the place of FPIES as a distinct clinical entity will be discussed.

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HISTORICAL BACKGROUND AND DEFINITION OF FPIES

In 1967, Gryboski (15) described a series of 21 children diagnosed with gastrointestinal symptoms of CMA. Most of the children began to experience symptoms during the first 6 weeks of life. Eleven of 21 had growth retardation, and 7 of 21 experienced symptoms of shock after reintroduction of the causal protein. Almost all the infants tolerated cow's milk by 3 years of age. A decade later, Powell (16) described two premature infants with symptoms of recurrent vomiting, bloody diarrhea, and abdominal distension with suspected necrotizing enterocolitis. For these two infants, no bacterial pathogens or other causes of necrotizing enterocolitis could be identified. However, both infants experienced resolution of their symptoms when not ingesting cow's milk or soybean infant formula, and both had recurrence of symptoms (vomiting, bloody diarrhea, and malabsorption) and elevation of their peripheral polymorphonuclear (PMN) leukocyte count when these formulas were reintroduced (casein hydrolysate formula was tolerated).

In a subsequent study, Powell (11) described nine infants with severe, protracted diarrhea and vomiting. The symptoms developed 4 to 27 days after birth (mean, 11 days) while the infants were consuming a cow's milk-based formula. Switching to a soybean-based formula resulted in transient improvement, but symptoms generally recurred in 7 days. Seven of the nine infants were below birth weight, and eight of nine had dehydration. Eight of the infants appeared acutely ill and underwent sepsis evaluations (negative). All infants were noted to have low serum albumin and an elevated PMN leukocyte count and stools were positive for heme and reducing substances. The hospital course for these infants usually involved improvement after administration of intravenous fluids, followed by recurrence of dramatic symptoms with reintroduction of soy- or cow's milk-based formula, including shock in several patients. Formal follow-up oral challenges were performed with cow's milk and soybean (30-100 ml of formula) at a mean age of 5.5 months. Fourteen of the 18 challenges elicited positive responses. Ten of 14 challenges resulted in vomiting (onset, 1-2.5 hours after ingestion; mean, 2.1 hours), and all experienced diarrhea (onset, 2-10 hours; mean, 5 hours) with blood, leukocytes, eosinophils, and increased carbohydrate in the stool. There was an increase in PMN leukocyte count in all positive challenges, peaking 6 hours after ingestion with a mean increase of 9,900 cells/mm³ (range, 5,500-16,800 cells/mm³). Only gastrointestinal symptoms were reported.

The results of these studies (11,16) led Powell to propose a particular challenge protocol (Table 1) and criteria for a positive oral challenge to diagnose food protein-induced enterocolitis of infancy (Table 2) (12). Powell recognized that other causes of symptoms that could mimic FPIES must be ruled out (infections, inflammatory bowel disease, ischemia, and others) and that normal weight gain and abatement of symptoms could be expected to occur when these infants were ingesting a hydrolyzed formula.

Table 1

Table 2

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CASE REPORT: AN EXAMPLE OF COW'S MILK-INDUCED ENTEROCOLITIS

The patient was a full-term male infant who was initially fed with a cow's milk-based formula. Between 7 and 14 days of age, progressive vomiting developed, with heme-positive diarrhea, and subsequent lethargy. He was admitted for a full sepsis evaluation (negative), and the symptoms resolved after he underwent intravenous hydration. He was discharged from the hospital with a soybean-based formula that was tolerated in the hospital. Because of mild symptoms of colic, at 8 weeks of age the formula was switched to a casein hydrolysate. Two hours after a first feeding of this formula, protracted vomiting occurred, and the soybean-based formula was therefore resumed. Accidental ingestion of a small amount of cow's milk at 5 months of age resulted in protracted vomiting (1 hour later), diarrhea (6 hours later), and acidemia and cyanosis requiring hospital admission. Milder symptoms occurred after ingestion of a tiny amount of cheese at 11 months of age.

The patient successfully avoided cow's milk from 11 months to 6 years of age. Results of prick skin tests and radioallergosorbent test (RAST) for cow's milk were negative. He was admitted to the hospital, and intravenous access was obtained. He received 1 oz (approximately 0.06 g/kg) of cow's milk protein in a single-blind challenge. He was without symptoms until 90 minutes after the ingestion, when abdominal pain and repetitive vomiting began and continued for 3 hours. At that time the peripheral blood PMN leukocyte count (including immature forms) had increased by 14,713 cells/mm³. There were no skin or respiratory symptoms. The diastolic blood pressure decreased by 10 mmHg. He was treated with intravenous fluids and then intravenous steroids. Symptoms resolved, and he was discharged home. Loose stools were noted the next day.

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CLINICAL CHARACTERISTICS

To summarize the observations of Powell (11,12,16), infantile FPIES is a severe syndrome of vomiting and diarrhea caused by milk and/or soy in infants. Confirmation of the allergy includes a negative search for other causes, improvement when not ingesting the causal protein, and a positive response to oral challenge, as described. Infants with symptoms consistent with severe enterocolitis who fulfilled, or are highly likely to have fulfilled, these criteria are included in many reports of milk or soy allergy of infancy (17-24). Some additional information about the clinical characteristics of these infants has emerged (Table 3). In a review of 17 infants admitted to hospitals with FPIES, Murray and Christie (25) reported six infants with acidemia (mean pH 7.03) and methemoglobinemia. It was hypothesized that this resulted from increased heme oxidation caused by an elevation of nitrites in the intestine. This elevation of nitrites can occur with severe intestinal inflammation, resulting in reduced catalase activity. The association of methemoglobinemia with FPIES was noted in the current case report and in our published experience with FPIES (13).



Table 3

Several other clinical features of infantile FPIES have emerged from our studies (13) (16 patients) and a study by Burks et al. (24) (43 patients). All the infants studied had negative skin-prick and/or RAST responses to the causal proteins (cow's milk and/or soy). Approximately half the infants reacted to both milk and soy. Sensitivity to milk was lost in 60% and to soy in 25% of the patients after 2 years from the time of initial occurrence. Lastly, while Powell challenged with approximately 0.6 g protein/kg body weight, in children with severe prior reactions as described in the current case report, lower doses may be adequate (0.06-0.6 g/kg).

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ATYPICAL DISEASE

Powell noted (12) that her strict challenge criteria for infantile FPIES would potentially exclude some patients who might have a similar or identical clinical manifestation or underlying pathophysiology but with differences in particular specific features or severity. Additionally, some patients who fulfill the challenge criteria may have particular features that do not satisfy the general description of infantile FPIES (13): reactions to foods other than cow's milk or soy, onset of symptoms beyond 9 months of age, and development or presence of IgE antibody directed toward the causal protein. For example, symptoms consistent with FPIES in infants have been described with foods including rice (26), poultry (13,27), fish (28), and pea (13). Similar to the patient described earlier, some patients with FPIES have experienced reactions to the residual protein in hydrolyzed cow's milk formula (13,29). Onset of FPIES outside of infancy may also occur (13). Lastly, we (13) have noted two patients who had typical infantile FPIES with negative skin-prick and RAST test results in whom positive test results were obtained 1 and 3 years after the diagnosis. In addition, three patients with positive skin-prick responses and RAST results to soybean (ages 7 months, 1 year, 9 years) showed only symptoms consistent with FPIES when orally challenged with soy. All five of these patients who eventually showed or had shown IgE antibody to the causal protein remained sensitive.

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DIAGNOSIS AND MANAGEMENT

As noted, the diagnosis rests on clinical and challenge criteria. In practicality, many patients would not undergo a formal challenge as infants because the diagnosis becomes self-evident after elimination of the causal protein. Unfortunately, this has been a hindrance to better studies of this syndrome. For treatment, as noted earlier, most infants do well consuming a casein hydrolysate formula. Because there is a high percentage of patients with sensitivity to both cow's milk and soy, switching directly to a hydrolysate is recommended. For the rare patients reactive to hydrolysate, an amino acid-based formula is appropriate (29). Families must be instructed about the careful avoidance of cow's milk or soy. Lists containing code words indicating cow's milk protein (i.e., casein, whey, natural flavoring, and others), and soy should be provided.

Follow-up challenges should be performed at intervals to determine tolerance (approximately every 18-24 months, depending on the clinical severity). These challenges should be performed under a physician's supervision with emergency medications immediately available, because dramatic reactions, including shock, can occur. Re-evaluation for development of antigen-specific IgE antibody may be helpful (13). Our (13) experience has been that approximately half of positive challenges require treatment (usually intravenous fluids). Because of the presumed pathophysiology, corticosteroids have been administered for severe reactions. The role of epinephrine for treatment is not known, but it should be available for severe cardiovascular reactions.

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HISTOLOGIC FINDINGS

Unfortunately, because infantile FPIES is a diagnosis that can be made clinically, there are no series in which biopsies have been performed solely in patients fulfilling Powell's criteria. Thus, specific descriptions of the histologic findings are not available, and only assumptions can be drawn by considering descriptions from case reports or series that probably included these patients. The findings from endoscopy and biopsy in FPIES are non-specific. Colonic specimens in symptomatic patients reveal crypt abscesses and a diffuse inflammatory cell infiltrate with prominent plasma cells, and small bowel specimens reveal edema, acute inflammation and mild villus injury (15,30-33). In some cases, focal erosive gastritis and esophagitis are found, with prominent eosinophilia and villus atrophy (31,34,35).

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PATHOPHYSIOLOGY

Van Sickle et al. (36) studied patients fulfilling Powell's strict criteria for FPIES and noted that in vitro stimulation of peripheral blood mononuclear cells with the causal antigen resulted in greater cell proliferation than in children with negative challenges. Also, an increase in serum antigen-specific IgA has been noted in these patients (37). The pathophysiologic ramifications and clinical implications of these findings remain unanswered. In other studies in patients who may have fulfilled the criteria for FPIES, a number of interesting observations have been made. Morphologic studies of the intestine show an increase of IgG- and IgM-containing plasmacytes, as well as an increase of intraepithelial lymphocytes (21). However, the presence of plasmacytes may be the result of a nonspecific immune response caused by an increased passage of antigen through the gut mucosa. The immune response to antigen in the gastrointestinal tract may primarily involve T cells. Cytokines secreted by activated T cells significantly influence the integrity of the mucosal barrier of the gut on exposure to the antigen. Heyman et al. (22) demonstrated that tumor necrosis factor (TNF)-[alpha] secreted by circulating milk protein-specific T cells increased intestinal permeability, thus contributing to the influx of antigen into the submucosa with further activation of antigen-specific lymphocytes. Fecal TNF-[alpha] was also found in increased concentrations after positive milk challenge in patients with enterocolitis (38). Benlounes et al. (23) showed that significantly lower doses of intact cow's milk protein stimulates TNF-[alpha] secretion from peripheral blood mononuclear cells of patients with active intestinal CMA, compared with patients whose sensitivity resolved or with those with skin, rather than intestinal, manifestations of cow's milk hypersensitivity. Interferon (IFN)-[gamma] significantly enhances the action of TNF-[alpha] on intestinal epithelial cells, and interleukin (IL)-4 has been determined to have a similar effect on the gut mucosa (39). Conversely, transforming growth factor (TGF)-[beta]1 protects the epithelial barrier of the gut from the penetration of foreign antigens by preventing the detrimental action of IFN-[gamma] (40).

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THE SYNDROME IN PERSPECTIVE

As has been described, infantile FPIES appears as a particularly severe gastrointestinal reaction to milk or soy protein. However, FPIES is also part of a clinical spectrum of non-IgE-mediated gastrointestinal food-allergic disorders. It may simply represent a more severe, generalized form of food-associated enteropathy, (14,23,41) proctocolitis, (31,42) or an earlier occurrence of eosinophilic gastroenteritis, (43) or it may be a distinct pathologic entity. The relationship of atypical FPIES to these food-allergic disorders remains to be clarified. It may be that older patients, even adults, with, for example, shellfish-induced vomiting and diarrhea in the absence of specific IgE antibody have a form of FPIES with a pathophysiologic basis similar to that of the infantile form. Clearly, further study (including histologic and immunologic correlates, and long-term clinical follow-up) of this and the other IgE and non-IgE-mediated food-allergic disorders affecting the gut is needed.

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REFERENCES

1. Bock SA. Prospective appraisal of complaints of adverse reactions to foods in children during the first 3 years of life. *Pediatrics* 1987;79:683-8. [Is it at Liverpool](#) | [\[Context Link\]](#)
2. Host A, Halken S. A prospective study of cow milk allergy in Danish infants during the first 3 years of life. *Allergy* 1990;45:587-96. [\[Context Link\]](#)
3. Hide DW, Guyer BM. Cow milk intolerance in Isle of Wight infants. *Br J Clin Prac* 1983;37:285-7. [Is it at Liverpool](#) | [\[Context Link\]](#)
4. Schrandt JJP, van den Bogart JPH, Forget PP, Schrandt-Stumpel CTRM, Kuijten RH, Kester ADM. Cow's milk protein intolerance in infants under 1 year of age: A prospective epidemiological study. *Eur J Pediatr* 1993;152:640-44. [Is it at Liverpool](#) | [\[Context Link\]](#)
5. Sicherer SH. Manifestations of food allergy: Evaluation and management. *Am Fam Phys* 1999;59:415-30. [Is it at Liverpool](#) | [\[Context Link\]](#)
6. Sampson HA. Food allergy. *JAMA* 1997;278:1888-94. [Is it at Liverpool](#) | [\[Context Link\]](#)
7. Host A, Jacobsen HP, Halken S, Holmenlund D. The natural history of cow's milk protein allergy/intolerance. *Eur J Clin Nutr* 1995;49(suppl 1):S13-S8. [Is it at Liverpool](#) | [\[Context Link\]](#)

8. Bock SA. The natural history of food sensitivity. *J Allergy Clin Immunol* 1982;69:173-7. [Is it at Liverpool](#) | [\[Context Link\]](#)
9. Trier JS. Celiac sprue. *N Engl J Med* 1991;325:1709-19. [Is it at Liverpool](#) | [\[Context Link\]](#)
10. Walker-Smith JA. Diagnostic criteria for gastrointestinal food allergy in childhood. *Clin Exp Allergy* 1995;25(suppl 1):20-2. [Is it at Liverpool](#) | [\[Context Link\]](#)
11. Powell GK. Milk- and soy-induced enterocolitis of infancy. *J Pediatr* 1978;93:553-60. [\[Context Link\]](#)
12. Powell G. Food protein-induced enterocolitis of infancy: Differential diagnosis and management. *Comp Ther* 1986;12:28-37. [Is it at Liverpool](#) | [\[Context Link\]](#)
13. Sicherer SH, Eigenmann PA, Sampson HA. Clinical features of food protein-induced enterocolitis syndrome. *J Pediatr* 1998;133:214-9. [Is it at Liverpool](#) | [\[Context Link\]](#)
14. Walker-Smith JA. Cow milk-sensitive enteropathy: Predisposing factors and treatment. *J Pediatr* 1992;121:S111-S5. [Is it at Liverpool](#) | [\[Context Link\]](#)
15. Gryboski J. Gastrointestinal milk allergy in infancy. *Pediatrics* 1967;40:354-62. [Is it at Liverpool](#) | [\[Context Link\]](#)
16. Powell GK. Enterocolitis in low-birth-weight infants associated with milk and soy protein intolerance. *J Pediatr* 1976;88:840-4. [Is it at Liverpool](#) | [\[Context Link\]](#)
17. Hill DJ, Firer MA, Shelton MJ, Hosking CS. Manifestations of milk allergy in infancy: Clinical and immunological findings. *J Pediatr* 1986;109:270-6. [Is it at Liverpool](#) | [\[Context Link\]](#)
18. Fontaine J, Navarro J. Small intestinal biopsy in cow's milk protein allergy in infancy. *Arch Dis Child* 1975;50:357-62. [Is it at Liverpool](#) | [\[Context Link\]](#)
19. Kuitunen P, Visakorpi J, Savilahti E, Pelkonen P. Malabsorption syndrome with cow's milk intolerance: Clinical findings and course in 54 cases. *Arch Dis Child* 1975;50:351-6. [Is it at Liverpool](#) | [\[Context Link\]](#)
20. Hill DJ, Firer MA, Ball G, Hosking CS. Natural history of cows' milk allergy in children: Immunological outcome over 2 years. *Clin Exp Allergy* 1993;23:124-31. [Is it at Liverpool](#) | [\[Context Link\]](#)
21. Perkkio M, Savilahti E, Kuitunen P. Morphometric and immunohistochemical study of jejunal biopsies from children with intestinal soy allergy. *Eur J Pediatr* 1981;137:63-9. [Is it at Liverpool](#) | [\[Context Link\]](#)
22. Heyman M, Darmon N, Dupont C, et al. Mononuclear cells from infants allergic to cow's milk secrete tumor necrosis factor alpha, altering intestinal function. *Gastroenterology* 1994;106:1514-23. [Is it at Liverpool](#) | [\[Context Link\]](#)
23. Benlounes N, Dupont C, Candalh C, et al. The threshold for immune cell reactivity to milk antigens decreases in cow's milk allergy with intestinal symptoms. *J Allergy Clin Immunol* 1996;98:781-9. [Is it at Liverpool](#) | [\[Context Link\]](#)
24. Burks AW, Casteel HB, Fiedorek SC, Williams LW, Pumphrey CL. Prospective oral food challenge study of two soybean protein isolates in patients with possible milk or soy protein enterocolitis. *Pediatr Allergy Immunol* 1994;5:40-5. [Is it at Liverpool](#) | [\[Context Link\]](#)
25. Murray K, Christie D. Dietary protein intolerance in infants with transient methemoglobinemia and diarrhea. *J Pediatr* 1993;122:90-2. [Is it at Liverpool](#) | [\[Context Link\]](#)
26. Borchers SD, Li BUK, Friedman RA, McClung HJ. Rice-induced anaphylactoid reaction (case report). *J Pediatr Gastroenterol Nutr* 1992;15:321-4. [Ovid Full Text](#) | [Is it at Liverpool](#) | [\[Context Link\]](#)
27. Vandenplas Y, Edelman R, Sacre L. Chicken-induced anaphylactoid reaction and colitis. *J Pediatr Gastroenterol Nutr* 1994;19:240-1. [Ovid Full Text](#) | [Is it at Liverpool](#) | [\[Context Link\]](#)
28. Vitoria JC, Camarero C, Sojo A, Ruiz A, Rodriguez-Soriano T. Enteropathy related to fish, rice and chicken. *Arch Dis Child* 1982;57:44-8. [Is it at Liverpool](#) | [\[Context Link\]](#)
29. Kelso JM, Sampson HA. Food protein-induced enterocolitis to casein hydrolysate formulas. *J Allergy Clin Immunol* 1993;92:909-10. [Is it at Liverpool](#) | [\[Context Link\]](#)
30. Goldman H, Provjansky R. Allergic proctitis and gastroenteritis in children. *Am J Surg Pathol* 1986;10:75-86. [Ovid Full Text](#) | [Is it at Liverpool](#) | [\[Context Link\]](#)

31. Lake AM. Food protein-induced colitis and gastroenteropathy in infants and children. In: Metcalfe DD, Sampson HA, Simon RA, eds. *Food allergy: Adverse reactions to foods and food additives*. Boston: Blackwell Scientific Publications, 1997:277-86. [\[Context Link\]](#)
32. Halpin TC, Byrne WJ, Ament ME. Colitis, persistent diarrhea, and soy protein intolerance. *J Pediatr* 1977;91:404-7. [Is it at Liverpool](#) | [\[Context Link\]](#)
33. Jenkins H, Pincott J, Soothill J, Milla P, Harries J. Food allergy: The major cause of infantile colitis. *Arch Dis Child* 1984;59:326-9. [Is it at Liverpool](#) | [\[Context Link\]](#)
34. Forget PP, Arenda JW. Cow's milk protein allergy and gastroesophageal reflux. *Eur J Pediatr* 1985;144:298-300. [Is it at Liverpool](#) | [\[Context Link\]](#)
35. Coello-Ranuez P, Larrosa-Haro A. Gastrointestinal occult hemorrhage and gastroduodenitis in cow's milk protein intolerance. *J Pediatr Gastroenterol Nutr* 1984;3:215-8. [Ovid Full Text](#) | [Is it at Liverpool](#) | [\[Context Link\]](#)
36. Van Sickle GJ, Powell GK, McDonald PJ, Goldblum RM. Milk- and soy protein-induced enterocolitis: Evidence for lymphocyte sensitization to specific food proteins. *Gastroenterology* 1985;88:1915-21. [\[Context Link\]](#)
37. McDonald PJ, Goldblum RM, Van Sickle GJ, Powell GK. Food protein-induced enterocolitis: altered antibody response to ingested antigen. *Pediatr Res* 1984;18:751-5. [Ovid Full Text](#) | [Is it at Liverpool](#) | [\[Context Link\]](#)
38. Majamaa H, Miettinen A, Laine S, Isolauri E. Intestinal inflammation in children with atopic eczema: Faecal eosinophil cationic protein and tumour necrosis factor-alpha as non-invasive indicators of food allergy. *Clin Exp Allergy* 1996;26:181-7. [Is it at Liverpool](#) | [\[Context Link\]](#)
39. Colgan S, Resnick M, Parkos C, et al. IL-4 directly modulates function of a model human intestinal epithelium. *J Immunol* 1994;153:2122-9. [Is it at Liverpool](#) | [\[Context Link\]](#)
40. Planchon S, Martins C, Guerrant R, Roche J. Regulation of intestinal epithelial barrier function by TGF-beta 1. *J Immunol* 1994;153:5730-9. [Is it at Liverpool](#) | [\[Context Link\]](#)
41. Walker-Smith JA. Food sensitive enteropathies. *Clin Gastroenterol* 1986;15:55-69. [Is it at Liverpool](#) | [\[Context Link\]](#)
42. Lake AM, Whittington PF, Hamilton SR. Dietary protein-induced colitis in breast-fed infants. *J Pediatr* 1982;101:906-10. [Is it at Liverpool](#) | [\[Context Link\]](#)
43. Min K-U, Metcalfe D. Eosinophilic gastroenteritis. *Immunol Allergy Clin N Am* 1991;11:799-813. [Is it at Liverpool](#) | [\[Context Link\]](#)

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Section Description

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IMAGE GALLERY

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Verify normal weight gain, no gastrointestinal symptoms while not ingesting causal protein.
Obtain baseline stool sample and peripheral blood polymorphonuclear leukocyte count.
Place intravenous catheter.
Prepare emergency medications (normal saline, corticosteroids, epinephrine).
Administer challenge (see text for dosage).
Observe for symptoms (usual onset 1–4 hours).
Repeat peripheral blood polymorphonuclear leukocyte count 6 hours after ingestion.
Collect subsequent stools for 24 hours.
Protocol from references 12 and 13.

Table 1

Symptoms (vomiting, diarrhea)
Fecal blood (gross or occult)
Fecal leukocytes
Fecal eosinophils
Increase in peripheral polymorphonuclear leukocyte count ($>3,500$ cells/mm ³).
Positive challenge: three of five criteria positive
Equivocal: two of five criteria positive

Table 2

Occurs in infants (onset usually in first month)
Severe vomiting, diarrhea (stools, leukocyte, reducing substance positive)
Failure to thrive
May appear to be "septic."
Resolves when causal protein (cow's milk, soy) discontinued.
Reaction to both milk and soy is at least 50%.
Low serum albumin
Methemoglobinemia, acidemia, shock may develop.
Negative immunoglobulin E antibody to milk and soy (skin prick and/or radioallergen sorbent test)
Most resolve within 2 years (milk sooner than soy allergies)
Features from references 12, 13, 24, and 31.

Table 3

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TABLE 1

Verify normal weight gain, no gastrointestinal symptoms while not ingesting causal protein.
 Obtain baseline stool sample and peripheral blood polymorphonuclear leukocyte count.
 Place intravenous catheter.
 Prepare emergency medications (normal saline, corticosteroids, epinephrine).
 Administer challenge (see text for dosage).
 Observe for symptoms (usual onset 1–4 hours).
 Repeat peripheral blood polymorphonuclear leukocyte count 6 hours after ingestion.
 Collect subsequent stools for 24 hours.

Protocol from references 12 and 13.

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TABLE 1 . Challenge protocol for food protein-induced enterocolitis syndrome

TABLE 2

Symptoms (vomiting, diarrhea) Fecal blood (gross or occult) Fecal leukocytes Fecal eosinophils Increase in peripheral polymorphonuclear leukocyte count ($>3,500$ cells/mm³). Positive challenge: three of five criteria positive Equivocal: two of five criteria positive
Criteria from reference 12.

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TABLE 2 . Criteria for a positive oral challenge

TABLE 3

Occurs in infants (onset usually in first month)
 Severe vomiting, diarrhea (heme, leukocyte, reducing substance positive)
 Failure to thrive
 May appear to be “septic.”
 Resolves when causal protein (cow’s milk, soy) discontinued.
 Reaction to both milk and soy in at least 50%
 Low serum albumin
 Methemoglobinemia, acidemia, shock may develop.
 Negative immunoglobulin E antibody to milk and soy (skin prick and/or radioallergosorbent test)
 Most resolve within 2 years (milk sooner than soy allergy)

Features from references 12, 13, 24, and 31.

Food Protein-Induced Enterocolitis Syndrome: Clinical Perspectives.

Sicherer, Scott

Journal of Pediatric Gastroenterology & Nutrition. 30(1) Supplement:S45-S49, January 2000.

TABLE 3 . Features of food protein-induced enterocolitis syndrome